Lec 3 Clinical
د/ نجوى

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"إن لم يبنه الرب البيت فباطلا تتعب البنائين"

①

« Clinical »

Lec 3
د/ نجوى
1/10

« Urinary tract Infections »

موضوع المحاضرة النهاردة سهل جداً وعرفنيه عنه كتير فمتقلقوش خالص.

"The term urinary tract infection (UTI) usually refers to the presence of organisms in the urinary tract together with signs and symptoms of inflammation"

وطبعاً مادام الـ UT فيه organisms يبقى بالتالى الـ urine هينزل فيه شوية من الـ organisms دى. بس احنا "أصلاً" عارفين ان الـ urethra (وهى القناه بين الـ bladder والـ opening لخارج الجسم) بيكون فيها bacteria عايشة فيها ومش بتسبب مشاكل. سواء كانت الـ bacteria دى normal flora او Contaminant على الـ urethra ومش عاملة مشاكل.
يبقى بالتالى اى عينة urine لازم يكون فيها نسبة bacteria بس الـ bacteruria دى ساعات بتكون significant to UTI وساعات بنعتبرها Contamination عادى.
تعالوا نقول الكمية دول.

* Significant Bacteruria:

Presence of at least 100,000 bacteria/ml of urine

However Counts of < 100,000 bact/ml are normally considered to be uretheral contaminants because small numbers of bacteria are normally found in the anterior urethra and may be washed out in urine samples.

يعنى وجدوا ان وجود significant bacteruria مش دايماً بيصاحبه اعراض الـ UTI
وبناءً على تعريف الـ UTI اللى فوق يبقى مانقدرش نعتبره UTI

* Asymptomatic Bacteriuria:

Significant bacteriuria in the absence of symptoms in the patient.

- تعالوا دلوقتي ناخد شوية terms كده متعلقين بموضوعنا علشان نفهم معناهم.

• Cystitis:

It's a syndrome of frequency, dysuria & urgency, which usually suggests injection restricted to the lower UT.

n.b: frequency: ⟵ معناها بيروح الحمام كتير
urgency: ⟵ بيحس انه لازم يروح حالاً.
dysuria: ⟵ painful urination.

• Acute pyelonephritis:

an acute injection of one or both kidneys.

• Chronic pyelonephritis:

Type of pathology of the kidney.

• Relapse & reinfection:

Both means recurrence of urinary inflammation

طيب امال ايه الفرق ؟؟

Relapse: recurrence caused by the SAME organism that caused the original injection

Reinfection: recurrence caused by a DIFFERENT organism and is a new injection.

The Epidemiology in

يعني نسبه حدوثه في الناس .
الدكتورة قالت انه النسب والارقام مش محفوظ . اعرف بس
بيجي مليه الكتر وكدة يعني .

- In infants up to the age of 6 months is much more common in boys more than girls.

- In preschool children, UTI becomes more common and the sex ratio reverses → 4.5% in girls
  ↘ 0.5% in boys.

- In older children, the prevelance of bacteruria is 1.2% among girls & 0.03% in boys.

- Up to 5% of adult women report that they had symptomatic UTI at some time.

- UTI is uncommon in young healthy men.

- In the elderly of both sexes the prevelance of bacteruria rises: 20% in women & 10% in men.

ده كلام الـ Slide بالظبط . دلوقتي هحاول الم الدنيا سُوبيّة :

- Infants (≤ 6 months) boys > girls.
- Children
  - Preschool : UTIs ↑↑ but girls > boys.
  - Older children : UTIs ↓ girls > boys

يعني داعياً البنات اكتر من الولاد ما عدا في الـ infants.

- Adults : women > men
- Elder people : UTIs ↑↑ women > men.

* Aetiology:

- Escherichia Coli is responsible for about 80% of UTI.
- the remaining 20% are caused by other G-ve bacteria as Klebsiella and Proteus species and by G+ve Cocci as enterococci and Staphylococcus saprophyticus
- UTI associated with underlying structural abnormality is often caused by more resistant organisms as:
  - Pseudomonas aeruginosa
  - Enterobacter species.
  - Serratia species.

  implicated in hospital acquired urinary infections, including those in patients with urinary Catheters.
- Rare causes of urinary infection include anaerobic bacteria and fungi.
- A number of viruses are excreted in urine but symptomatic infection is Confined to immunoCompromised patients patients. particularly children following bone marrow transplantation in whom adenoviruses & polyomaviruses are associated with haemmorrhagic Cystitis

- بصوا بالنسبه للاسماء. احفظوا مثل واحد لكل نوع. ماعدا اسامى الـ Viruses نحفظ الاسميه.

- بالنسبه لثالث نقطه. دى معناها ان الشخص ده كان عنده اصلاً مشكلة فى الـ Structure بتاع الـ urinary system وموجود فى المستشفى وعلشان يكون عامل urinary Catheter ده بيعطيه infection بس بنوع اقوى من الـ organisms

Pathogenesis:

تحت العنوان ده هتكلم عن: ١- الحاجات اللى عند ال organism بتساعده على انه يعمل infection
- الحاجات اللى عند ال host اللى بتساعده على المقاومة
- العيوب اللى عند ال host اللى عليه تمنعه من المقاومة
او تساعد على حدوث ال infection (معرفتى انا مثلاً)

1] The organism:

Some strains of E.coli possess certain virulence factors that enhance their ability to cause infection, including:

* Bacterial surface structures called P. fimbrie: help in the adherance of bacteria to the glycolipid receptors on renal epithelial cells.
يعنى حاجات كده زى الحبال طالعة من ال bacteria بتقدر تثبت الbacteria فى ال renal epithelial cells

- Possession of the iron scavenging aerobactin system.
مش عارفة دى ايه بالظبط

- Increased amounts of Capsular K antigen for the resistance of phagocytosis by WBCs of the host.

2] The Host:

- Although many bacteria can readily grow in urine, however the high urea concentration and extremes of osmolality & pH inhibit growth somehow.

- the flushing mechanism of bladder emptying, since the small numbers of bacteria finding their way into the bladder are elimenated

when the bladder is emptied.
يبقى ال organisms بيطرد ال bladder من ال urine يعني خروج خارج الجسم

3- The bladder mucosa is intrinsically resistant to bacterial adherence. but in sufficient numbers, bacteria with strong adhesive systems can overcome this defense.

4. When the bladder is injected, WBCs are mobilized to the bladder surface to ingest and destroy invading bacteria.

3] Abnormalities of the UT that increase suciptibility to infection:

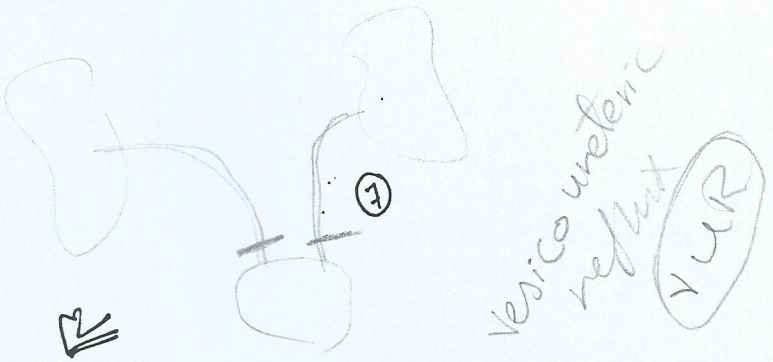
① Any structural abnormality leading to the obstruction of flow and urinary stasis increases the likehood of infection.

Such abnormalities include: عيوب خلقية
- Congenital anomalies of the ureters or urethra
- Renal stones
- Enlargement of prostate in men.

* Renal stones can be infected with bacteria as Proteus & Klebsiella species and become (~~infect~~) a source of relapsing infection.

يعني الـ renal stones دي مش بس بتسد خروج الـ urine فبتساعد على الـ infection لأن دي كمان عكسة مرتفعة تستخبى فيها الـ organisms وبعد فترة تطلع منها وتعمل relapse.

اقلبوا الصفحة علشان تعرفوا مرض تاني عكسة بيساعد على حدوث الـ UTI.



Vesicoureteric reflux (VUR):

It's a condition caused by failure of physiological valves at the function of the ureters and the bladder.

∴ When the bladder contracts, urine reflux back towards the kidney.

It's probable that VUR plays an important role in childhood UTI that lead to → Chronic renal damage (scarring)
↘ Persistence of infection.

يعني من الآخر الـ valves اللي بين الـ ureters اللي جاية من الكلى والـ Bladder باظبط وبالتالي الـ urine بقى يرجع تاني لفوق للـ kidney وطبعاً ده بيبوظ الكلى خالص. وبيساعد على الـ infection.

كل ده اجنا تحت عنوان Pathogenesis. هندخل دلوقتي على عنوان جديد.

Clinical Manifestations

Most UTI are asymptomatic.
Symptoms (when they occur) are result of irritation of the bladder and urethral mucosa.

يعني في اوقات كتير بيكون فيه infection بس من غير symptoms. طيب الـ symptoms دي بتكون نتيجة ايه؟ نتيجة irritation للـ mucosa بتاعة الـ Urethra Bladder وطبعاً الـ infection هو اللي بيعمل الـ irritation دي.

تعالوا دلوقتي نتكلم عن الـ Clinical manifestations في كل نوع من الـ populations.

* Babies & infants:

Symptoms include vomiting, fever, & diarrhea.

UTI in infancy and childhood is a major risk factor for the development of renal scarring associated with chronic pyelonephritis in adulthood, hypertension & renal failure.

يعني خطورة إن الطفل ده يعمله UTI هو إنه ليه Complications وحشة على الكلى ومعلش يؤدي لما يكبر لحالة renal failure علشان كده لازم نعالجه كويس

* Children:

Above the age of 2 with some of the classical symptoms as frequency, dysuria and haematuria

Some children present with acute abdominal pain and vomiting.

* Adults:

Symptoms of:
- lower UTI: Frequency, urgency, dysuria and Haematuria
- Upper UTI: Fever.

* Elderly patients:

- Majority of cases are asymptomatic and even when present, symptoms are not diagnostic because frequency, dysuria, hesitancy and incontinence are fairly common in elder people without infection.
علشان الكبار دول ممكن UTI عندهم ال symptoms دي.
- UTI is one of the most frequent causes of admission to hospital among the elderly.

Investigation:

- Successful lab diagnosis of UTI lies in obtaining an uncontaminated urine sample for microscopy & Culture.

Contaminating bacteria can be from skin, Vaginal flora in women and penile flora in men

- the urine sample must be a midstream urine sample (MSU) (it's less contaminated)

فكره الـ MSU ان العينة بتكون من غير اول شوية من الـ urine اللي بتيجي. بيكون فيها organisms في الـ urethra بينزلوا في الاول. وآخر حبه برضه بيكون فيها الـ organisms اللي في الـ Bladder ملتش كدة احسن حاجة اكيد اللي في النص.

* this requires: (for collecting a sample)

1) Careful cleansing of the perineum & external genitalia with soap & water

2) Controlled micturition in which only the middle portion is collected, the initial & final portion being voided in toilet or bedpan

* Specimens: must reach the lab within 2 hrs or should be refrigerated otherwise any bacteria in the specimen will multiply & might give rise to a false +ve result.

يعني لو العينه مش هتروح المعمل على طول بعد بالكتير ساعتين لازم تحط العينه في الثلاجة علشان توقف نمو البكتيريا وإلا هتتدينا False +ve Bacteria طبيب عمله نعمل ايه كلام علشان توقف نمو الـ

Methods of overcoming bacterial multiplication in urine include the addition of boric acid to the container.

Rx

يعني يحطوا boric عشان يمنعوا تكاثر الـ Bacteria
فيه بقى كام اقتراح تانى عشان لو هتاخد العينة ومش
هتزرعها المعمل على طول.. انك تحط فى العينه حاجه كده اسمها
agar-coated paddle عبارة عن حاجة على شكل
الـ paddle كده مغموسه agar نحطها فى العينة فتعمل Culture
للبكتيريا على بال ما نروح المعمل.. يعنى الـ bacteria تتوجلهم مزروعة
جاهزة (يا سلام على الدلع)

ده طبعاً مسبباش احنا كلنا عندنا فى البيت Boric acid متوفر
و الـ agar متوفر فى كل حته فى الشقه عندنا.. ماعلينا

The use of dipslids in which an agar-coated paddle is dipped into the urine and submitted directly to the lab for incubation.

فيه ناس تانية ماشيه على منهج تانى فى الـ investigation تعالوا نشوف

Some advocate the policy of empirical antimicrobial Rx in the 1st instance and reserve the investigations to those who who do not respond.

يعنى اول ما يحسوا ان المريض عنده U.T.I يبدأوا Ab empirical يعنى
حاجة كده عمياني من غير ما يعملوا sensitivity tests ولو المريض
ما استجبش للعلاج يبقى بقى ساعتها يعملوا Culture و investigate
وكل اللى هم عايزينه..

Others are in favour of using cheaper, more convenient screening tests for ex.: urine dipstick for Blood & leukocyte esterase, these tests are reliable only when applied for fresh urine samples.

يعنى فيه ناس بتشوف ان الـ Culture والحاجات دى تاخد
وقت كتير فبيستعملوا الـ dipsticks زى
بتاعة الكرية بس بتكشف الدم او الـ Leucocyte esterase
فى الـ urine.
تعالوا نشوف ايه
الـ enzyme ده.

Leucocyte esterase is an enzyme released by WBCs. its presence in urine indicate significant bacteruria (>100,000 bact./ml)

- طيب ايه طرق الـ investigations تاني؟
- A valid alternative is just to hold the specimen up to the light specimens that are visibly clear are very likely to be sterile.

يعني في الغالب عينة البول اللي infected بتكون turbid بس طبعاً دي طريقة ما ينفعش نعتمد عليها لوحدها.

- تعالوا نتكلم شوية عن الـ Culture ...

* Culture:

Patients with UTI usually have at least 100,000 bacteria/ml, while in patients without infection the count is usually less.
However sometimes true infections may be associated with low counts particularly when: - the urine is diluted due to ↑ fluid intake
or - when the pathogen is slow growing.

يعني في الطبيعي العدد لازم يبقى أكتر من ١٠٠٠٠٠ لكن علشان العدد يكون اقل وفيه infection برده. ده في حالة إن الـ urine مخفف لأنه المريض بيشرب كتير مثلاً" او لأن الـ pathogen اللي عامل الـ UTI بينمو ببطء.

دلوقتي هنتكلم على العلاج وهنا فيه تحته ٧ عناوين هنشرحهم ...

Treatment

1- Non spicific III
2- Antimicrobial Chemotherapy
3- UnComplicated lower UTI
4- Acute Pyelonephritis
5- Relapsing UTI
6- Catheter associated infections
7- Bacteruria of Pregnancy.

Non specific Tt:

- Advising patients with UTI to drink alot of fluids is common practice on the theoritical bases that more infected urine is removed by frequent bladder emptying.

كل ما بشرب اكتر بنزل urine اكتر فبنظف ال UT من ال bacteria

- Urinary analgesics such as K or Na citrate which alkalinize the urine used as an adjunct to Abs.

However they shouldn't be used with nitrofurantoin as it's active only at acidic ptt.

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② Antimicrobial chemotherapy:

- select the agent with the narrowest possible spectrum and administer it for the shortest possible time.
- Blood level of Abs appear to be unimportant in the Tt of lower UTI, what matters is their concentration in urine.

However, Blood levels are probably important in treating pyelonephritis, which may progress to Bacteremia.

بس في الطبيعي ، المهم هو تركيز الدواء في الـurine لانه الـ conc. دي في الـ pyelonephritis هتموت الـ Bacteria اللي في الـ UT ماعدا في حالة الـ pyelonephritis لانه الـ infected هنا بيكون في الـ kidney فممكن يتنقل للدم لذلك تركيز الدواء في الدم مهم برده هنا.

* Drugs suitable for the oral Tt of cystitis include: (مهم)
  - β-lactams (Amoxicillin, Coamoxiclave & oral Cephalosporins)
  - Fluoroquinolones (Ciprofloxacin, Norfloxacin & OFloxacin)
  - Trimethoprim
  - Nitrofurantoin.

* IV drugs (for serious cases):
  - β-lactams (amoxicillin & Cefuroxime)
  - Quinolones (Ciprofloxacin)
  - Aminoglycosides (Gentamicin)

يس طبعاً لازم هنا تكون متأكد انه الكائن مقاوم كويس قبل ما تدي aminoglycoside.

- Penicillins and Cephalosporins attain satisfactory Concentrations and are relatively non toxic
∴ they are agents of choice for TT of UTI in the presence of renal failure.

③ Uncomplicated lower UTI TT: → bladder & urethra.

* Adults:
Quinolones are best reserved for TT failures and more difficult infections. بنسبة للحالات الصعبة.

• Other drugs include: - Cotrimoxazole
- Pivamecillinam
- Nalidixic acid.

However, Cotrimoxazole is now recognized as a cause of bone marrow depression & other hematological SEs.

• Duration of TT:
- Course of 7-10 days
- Single dose therapy with its advantages of cost, compliance and low SE but is less effective than when used for longer.
- in the urethral syndrome (infects limited to urethra), it's worth trying a 3 days course of one of the agents mentioned if this fails a 7 days course of tetracyclin could be tried to deal with possible Chlamydia or mycoplasma infection.

* Children:
- Drugs of choice: - β lactames - Trimethoprim - Nitrofurantoin.

✓ Quinolones are Contraindicated in children because of the risk of causing Cartilage & Joint problems.
- Children should be treated for 7-10 days.

βlactames - trimethoprim - Nitrofurantoin

④ Acute pyelonephritis:

Patients with pyelonephritis may be severly ill and if so, may require admission to hospital & initial IV with a parenteral Ab as:
- Cephalosporins (Cefuroxime & Ceftazidine)
- Some penicillins (Co amoxiclav)
- Aminoglycosides (Gentamycin)
- Quinolones

- A 1st choice agent would be parenteral Gentamycin or Ciprofloxacin.
. aminoglycosides: يجب ان نتأكد من ال kidney funct قبل ما نبدأ
- if the patient is improving, then the route of administration may be switched to oral therapy typicaly using a quinolone for 10-14 days.

* In hospital acquired pyelonephritis:
There is a risk that the injecting organism may be resistant to the usual 1st line d's.
Thus start a broad spectrum agent as Ceftazidime, Ciprofloxacin or meropenem.

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⑤ Relapsing UTI:

- Patients who fail on a 7-10 day course should be given a 2 week course & if that fails a 6 week course can be considered
ie: 7-10 days Fail → 2 weeks Fails → 6 weeks.
- Structural abnormality may need surgical correction before Cure can be maintained

مثال: لو عنده عيب خلقي مثلاً او اي حاجة بتساعد على ال infection
يبقى كل ما هاعالجه هيرجع يجيله تاني infection

⑥ Catheter associated infections:

- Even with the best catheter care, most will have infected urine after 10-14 days of catheterization.
  Most of these infections will be asymptomatic.
- Ab ttt will often eradicate the injecting organism but as long as the catheter remains in place, the organism or another more resistant one will quickly return.

* Principles of Ab therapy for catheter associated UTI are:

- Don't treat asymptomatic infection.
- If possible, remove the catheter before treating symptomatic infection.
- Following catheter removal, bacteruria may resolve spontaneously but more often it persists & may become symptomatic which responds well to single dose ttt.

بعض عكس بعد ما اشيل الـ Catheter الـ infected ممكن لو عمله كده هيتعالج الاحياء ما بيختفش وبيتحول لـ symptomatic.

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⑦ Bacteruria of Pregnancy:

- The prevalence of asymptomatic bacteruria of pregnancy is about 5% & $\frac{1}{3}$ of these women proceed to develope acute pyelonph.

طيب ليه اعراض الـ UTI بتبان اكتر؟

- Asymptomatic bacteruria is associated with:
  - low birth weight
  - Prematurity
  - HTN & pre-eclampsia.
- D's of choice: Amoxicillin, Cefalexin, Nitrofurantoin. } Depending on the sensitivity profile of the injecting organism.

- Co-Amoxiclav & Ciprofloxacin are cautioned in pregnancy because of lack of clinical experience in pregnant women.

يعني ميفرقوش اوى الادوية دى عكس تاثر سلبياً على الحمل ولا لا.

- Trimethoprim is Contraindicated because of its theoritical risk of causing neural tube defects
- 7 days !!! is the Standard duration.

n.b: ∞ Trimethoprim is CI in pregnants
& Quinolones are CI in children

ودلوقتى مع آخر عنوان فى حلقتنا النهاردة ...

Prevention & Prophylaxis:

- Cranberry Juice has been long thought to be beneficial in preventing UTI

محدش بقى يسألنى ليه عمو Cranberry اللى بيحبه الجمبرى ده.
اهو عصير وخلاص.

- In elderly women, a daily intake of 300 ml Cranberry Juice was associated with a halfing of the risk of bacteruria.

- If the reinjections are clearly related to sexual intercourse then a single dose of an Ab after intercourse is appropriate
- Long term, low dose prophylaxis may be beneficial.
- One dose of trimethoprim (100mg) or Nitrofurantoin (50mg) at night will suffice
- In children, recurrence of UTI is common & the complications potentially hazardous, so many clinicians recommend antimicrobial prophylaxis following documented infection.

قبل ماحشى عايزه بس اقولكم ان الحاجات المخطوط تحتها خط (غير الفارسى طبعاً) دى محولة بلون تانى فى الـ presentation وده معناه انها مهمة. يبقى تركز
(CM, KA)